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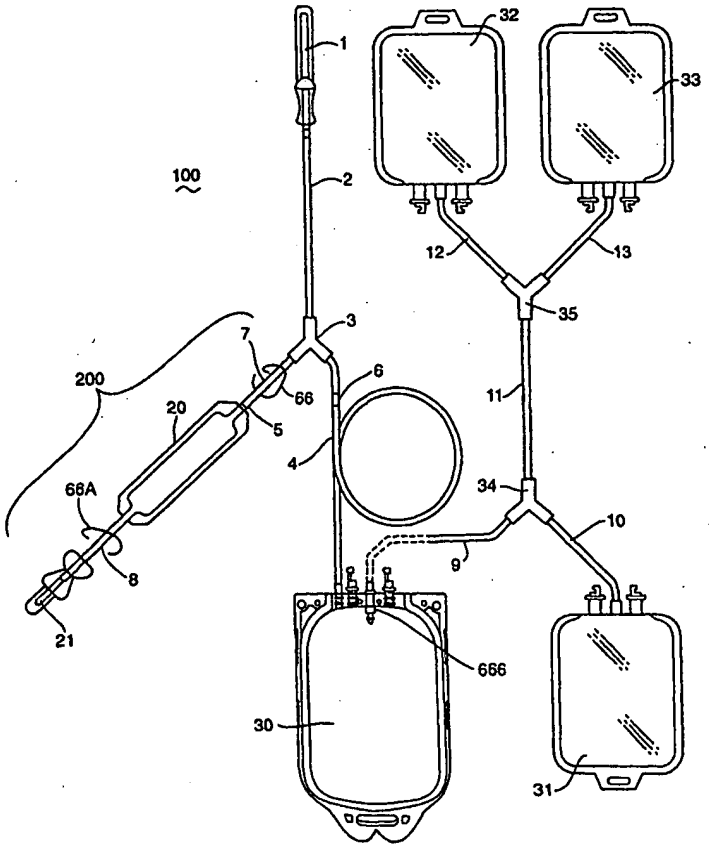
(54) Title: BIOLOGICAL FLUID PROCESSING SYSTEM

(57) Abstract

Systems for and methods minimizing bacterial contamination of biological fluid, particularly while allowing a portion of the biological fluid to be prepared (e.g., for testing) in a closed system, are disclosed. A system for processing a biological fluid (100) comprises a biological fluid collection device (200) for receiving a first portion of a biological fluid from a source of the biological fluid, the device being capable of being sealed while maintaining a closed system, at least a first container (30) for receiving a second portion of a biological fluid from the source of the biological fluid, wherein the biological fluid collecting device and the first container are in fluid communication with the source of the biological fluid.



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BIOLOGICAL FLUID PROCESSING SYSTEM

This application claims the benefit of U.S. provisional patent application 60/095,924, filed August 7, 1998, which is incorporated by reference.

TECHNICAL FIELD

This invention relates to the processing biological fluids such as blood and blood components, and particularly relates to minimizing contamination of the biological fluid with undesirable material such as bacteria, while allowing portions of biological fluid (e.g., for sampling) to be obtained in a closed system.

BACKGROUND OF THE INVENTION

Blood consists of a number of components having different characteristics and uses. Accordingly, blood is typically processed to separate the components to yield a variety of valuable blood products. For example, a unit of donated whole blood can be processed to separate red cells, usually concentrated as packed red cells (PRC), platelets, usually concentrated as platelet concentrate (PC), and plasma. In accordance with some processing protocols, blood can be treated to form platelet-rich-plasma (PRP) or buffy coat, before forming PC and/or separating plasma.

The separated components can be stored before being used as a blood product, particularly before being used as a transfusion product. Illustratively, PC can be stored for several days or more, and PRC can be stored for several weeks or more, before transfusion into a patient. Moreover, multiple units of some components, e.g., PC, buffy coat, and/or plasma, can be pooled before producing the final blood product.

Stored and/or non-stored components typically include undesirable material such as bacteria. Bacteria can contaminate the blood or blood component during blood collection and/or storage. One source of bacterial contamination may be the blood donor's skin, which may contain one or more varieties of bacteria, e.g., gram positive bacteria such as Staphylococcus epidermidis, and S. aureus, and/or gram negative bacteria. Other bacterial contaminants include, for example, coagulase negative staphylococci.

Since swabbing the donor's skin (e.g., with alcohol) prior to venipuncture may be inadequate to assure sterility, the bacteria may pass into the blood collection container,

and the bacteria may reproduce while the blood or blood component is stored. Additionally, some phlebotomy needles may cut a disc of skin when the phlebotomy needle is inserted into the donor, allowing the bacteria-containing skin plug to pass with the blood into the blood collection container.

The preparation of blood samples at the time of blood donation provides another potential route for contamination. For example, in accordance with some sampling protocols, the seal of a sampling device such as an evacuated blood collection tube is punctured by a needle or spike, and a portion of blood is passed from the donor (or from the collection container), through the needle, and into the sampling device. A plurality of sampling devices can be filled sequentially as desired. However, the use of a needle or spike can compromise the integrity of the blood processing system, as it provides an opening that creates the potential for contaminants (e.g., bacteria) to enter the system. As a result, subsequently collected blood (or blood previously collected in the container) can be contaminated by bacteria.

Some protocols for obtaining samples provide a potential route for contamination of the sample. For example, some protocols include cutting a conduit containing blood therein, and allowing the blood to "drip" into the sampling device. This opening can allow bacteria to contaminate the sample. Samples, as well as blood components prepared in open systems are not stored, and must be utilized (e.g., analyzed or transfused), or discarded, within 24 hours.

Since some blood components (e.g., platelets) are typically stored at ambient temperatures, the problem of contamination may be magnified, as some bacteria reproduce more rapidly at ambient temperatures. The administration of the bacterially contaminated transfusion product, particularly when the product contains massive bacterial contamination, may have adverse affects on the recipient. As a result, the United States currently prohibits the transfusion of platelet products that have been stored for more than 5 days, since platelets stored for 7 days are considered more likely to have massive bacterial contamination. Japan and Europe have similar, or even stricter, prohibitions. Additionally, fear of contamination is one reason that the United States prohibits the transfusion of pooled platelet products unless the platelets are transfused within four hours of pooling.

The present invention provides for ameliorating at least some of the disadvantages of the prior art. These and other advantages of the present invention will be apparent

from the description as set forth below.

SUMMARY OF THE INVENTION

Methods and systems according to the instant invention provide for obtaining a first portion (e.g., for use in providing at least one sample) of biological fluid in a closed system, and allow for obtaining a second portion of biological fluid while minimizing the presence of undesirable material such as bacteria in the second portion of biological fluid.

In a preferred embodiment, a first portion of a biological fluid such as blood drawn from a donor (that may include bacteria passed from the donor's skin and/or include the donor's bacteria-containing skin plug) is collected in at least one sealable biological fluid collecting device, and a second portion of the biological fluid (that is less likely to present a significant risk of bacterial contamination) is separately received, while maintaining the closed system, in a receiving container such as a blood bag. In some embodiments, at least one sealable biological fluid collecting device further comprises a cannula or needle, e.g., for penetrating the seal of a sampling device such as an evacuated blood collection tube after receiving biological fluid in the sealable collecting device.

Methods and systems according to embodiments of the invention provide for passing a first portion of biological fluid into a first collection device, and passing at least some volume of the first portion of the biological fluid from the first collection device into at least one additional (e.g., a second) collection device, wherein at least the first and second collection devices can be sealed while maintaining a closed system.

In accordance with another embodiment of the invention, a biological fluid collection arrangement is provided, comprising at least two biological fluid collection devices, communicating in series or in parallel, wherein the devices are capable of being sealed while maintaining a closed system. The arrangement can include additional biological fluid collection devices, communicating in series and/or in parallel, and the additional devices are typically capable of being sealed while maintaining a closed system.

Typically, the second portion of the biological fluid, e.g., donated whole blood, is processed to separate one or more components of interest (e.g., plasma, platelets, and/or red blood cells) to produce a variety of blood products. If desired, one or more components is depleted of leukocytes.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates an embodiment of a system according to the present invention, including a collection device for collecting a first portion of a biological fluid, and a receiving container such as a blood bag for receiving a second portion of the biological fluid.

Figure 2 illustrates another embodiment of a system according to the present invention, including a biological fluid collection arrangement comprising first and second collection devices in series for collecting a first portion of a biological fluid (the second collection device having a resilient wall), the system also including a receiving container such as a blood bag for receiving a second portion of the biological fluid.

SPECIFIC DESCRIPTION OF THE INVENTION

In accordance with an embodiment of the present invention, a method for processing a biological fluid comprises passing a first portion of a biological fluid into at least one collection device capable of being sealed while maintaining a closed system, and, while maintaining the closed system, passing a second portion of the biological fluid into a first container, e.g., a receiving container such as a blood bag. Preferably, the collection device containing the first portion of biological fluid is sealed and separated from the rest of the biological fluid processing system, and the first portion of biological fluid is sampled and/or analyzed. For example, embodiments of the method can include passing at least a part of the first portion of biological fluid from the collection device into a sampling device.

Preferably, the second portion of biological fluid is further processed, e.g., to provide separated components for use as transfusion products.

One embodiment of a biological fluid processing system according to the invention comprises at least one biological fluid collection device for receiving a first portion of a biological fluid from a source of the biological fluid, the device(s) being capable of being sealed while maintaining a closed system, and at least one container (e.g., a receiving container such as a first blood bag) for receiving a second portion of a biological fluid from the source of the biological fluid, while maintaining the closed system, wherein the biological fluid collection device and the first blood bag are in fluid communication with the source of the biological fluid. In some embodiments, a biological fluid collecting device further comprises a needle or cannula, e.g., for use with a stoppered evacuated

blood collection tube such as a vacutainer. Typically, the system also includes at least one flow control device, more preferably, at least one in-line valve.

Typically, the system includes at least one, and preferably, at least two, additional containers such as blood bags, e.g., for blood components and/or additives.

An embodiment of a device for processing a biological fluid comprises at least one reservoir for collecting biological fluid, and a conduit in fluid communication with the reservoir, wherein the device is arranged to receive a first portion of a biological fluid in a closed system. Preferably, the device is capable of being sealed while maintaining a closed system after receiving the first portion of biological fluid.

An embodiment of a biological fluid collection arrangement comprises at least a first collection device for receiving a first portion of biological fluid, and at least one additional collection device in fluid communication with the first collection device, wherein the first and additional collection devices can be sealed, after receiving biological fluid, while maintaining a closed system.

As used herein a biological fluid includes any treated or untreated fluid associated with living organisms, particularly blood, including whole blood, warm or cold blood, and stored or fresh blood; treated blood, such as blood diluted with at least one physiological solution, including but not limited to saline, nutrient, additive and/or anticoagulant solutions; blood components, such as platelet concentrate (PC), platelet-rich plasma (PRP), platelet-poor plasma (PPP), platelet-free plasma, plasma, components obtained from plasma, packed red cells (PRC), transition zone material or buffy coat (BC); blood products derived from blood or a blood component or derived from bone marrow; red cells separated from plasma and resuspended in a physiological fluid or a cryoprotective fluid; and platelets separated from plasma and resuspended in a physiological fluid or a cryoprotective fluid. The biological fluid may have been treated to remove some of the leukocytes before being processed according to the invention. As used herein, blood product or biological fluid refers to the components described above, and to similar blood products or biological fluids obtained by other means and with similar properties.

A "unit" is the quantity of biological fluid from a donor or derived from one unit of whole blood. It may also refer to the quantity drawn during a single donation. Typically, the volume of a unit varies, the amount differing from donation to donation. Multiple units of some blood components, particularly platelets and buffy coat, may be pooled or combined, typically by combining four or more units.

Each of the components of the invention will now be described in more detail below, wherein like components have like reference numbers.

The Figures illustrate embodiments of a closed biological fluid processing system 100 in accordance with the present invention. The exemplary illustrated embodiments of the system 100 include a needle or cannula 1 (shown with a removable needle cover), a first biological fluid collection device 200 for receiving a first portion of a biological fluid, a container 30 such as a blood bag for receiving a second portion of a biological fluid, wherein a plurality of conduits 2, 4, 5 and 8, and at least one connector 3, allow fluid communication between the components of the system. The illustrated embodiments of the system 100 include at least four flow control devices 6, 66, 66A, and 666.

In the embodiment illustrated in Figure 1, the biological fluid collection device 200 comprises at least one reservoir 20, at least two conduits 5, and 8, and also includes a needle or cannula 21, e.g., for penetrating the seal of a sampling device such as a vacutainer. The needle or cannula 21 is shown with a removable cover. As will be described in more detail below, in one preferred embodiment, after the collection device 200 containing the first portion of biological fluid is sealed (e.g., clamped and/or heat sealed), for example at location 7 of conduit 5, the needle or cannula 21 is inserted into a sampling device, and at least some volume of the first portion of biological fluid is passed into the sampling device.

In the embodiment of the system illustrated in Figure 2, the system includes a biological fluid collection arrangement comprising first and second biological fluid collection devices 200, 200A in series, the first collection device 200 comprising at least one reservoir 20, and at least one conduit 5, and the second collection device 200A comprising at least one reservoir 20A, having side walls 23, a reservoir cover or cap 22 (e.g., a removable cover for allowing access to the portion of biological fluid collected in the collection device), wherein the device 200A also includes at least one conduit 8. In one embodiment, after the first collection device 200 containing the first portion of biological fluid is sealed (e.g., conduit 5 is clamped and/or heat sealed), at least some of the volume of the biological fluid is passed from first collection device 200 (e.g., from reservoir 20) into second collection device 200A, and conduit 8 is sealed while maintaining a closed system. Subsequently (e.g., after storing the device 200A for a desirable period of time), cover 22 is removed, and at least some volume of the biological fluid is withdrawn from second collection device 200A for analysis. If desired, at least

some volume of the biological fluid is withdrawn from first collection device 200 for analysis.

The system can include additional elements such as, but not limited to, additional containers, conduits, and connectors. Typically, the system includes at least one additional container and conduit. The system can be included as part of any suitable biological fluid processing set. For example, the illustrated embodiments of system 100 show optional additional elements (connected to container 30 via partially dotted lines), e.g., conduits 9-13, containers 31-33, and connectors 34 and 35.

In accordance with the invention, the first and second portions of the biological fluid are collected while maintaining a closed system. As used herein, the term "closed" refers to a system that allows the collection and processing (and, if desired, the manipulation, e.g., separation of portions, separation into components, filtration, storage, and preservation) of biological fluid, e.g., donor blood, blood samples, and/or blood components, without the need to compromise the integrity of the system. A closed system can be as originally made, or result from the connection of system components using what are known as "sterile docking" devices. Illustrative sterile docking devices are disclosed in U.S. Patent Nos. 4,507,119, 4,737,214, and 4,913,756.

The components of the system may be constructed of any suitable material, and a wide variety of suitable materials are known in the art. Typically, the components are constructed from materials that are compatible with biological fluids and sterilization protocols. In a preferred embodiment, at least one of the components is compatible with heat-sealing protocols.

In some embodiments, at least one of the components is compatible with a biological fluid additive and/or preservative solution.

Preferably, the collection device reservoirs 20, 20A, the containers 30-33, the conduits 2, 4, 5, and 8-13, and the cap 22, are made from plasticized materials, e.g., plasticized polyvinyl chloride (PVC). Exemplary plasticized PVC materials include, but are not limited to, PVC plasticized with dioctylphthalate (DOP), diethylhelxylphthalate (DEHP), or trioctyltrimelliate (TOTM).

If desired, at least one collection device reservoir can be substantially flexible, e.g., it can collapse or deform when the reservoir is empty and is unsupported by external means. For example, the reservoir 20 shown in Figures 1 and 2 can be substantially flexible.

Alternatively, at least one reservoir can have sufficient rigidity that it does not collapse or deform when the reservoir is empty and is unsupported by external means. In some embodiments, at least a portion of the reservoir, (e.g., a side wall) is resilient. For example, the side walls 23 of reservoir 20A shown in Figure 2 can be resilient, and the reservoir can have sufficient rigidity that it does not collapse when empty. As used herein, the term "resilient" refers to the property of springing back, e.g., to regain, either fully, or approximately, an original position or shape after having been deformed, e.g., bent, stretched, or compressed. Illustratively, in some embodiments wherein the reservoir comprises a container having a plurality of side walls, or a continuous side wall, at least one wall (or a portion thereof) "springs back" to its previous position or shape after compression. Alternatively, or additionally, the reservoir comprises a container including a resilient end wall such as the bottom wall (or a portion thereof) that "springs back" to its previous position or shape after compression. Typically, the process of the wall springing back to its previous position creates a negative differential pressure in the reservoir, and this causes fluid to enter the reservoir.

The reservoirs 20, 20A, as well as the containers 30-33, can be of any suitable size and shape.

Typically, the reservoirs 20 and 20A are suitable for containing at least about 3 ml of biological fluid, e.g., in the range of from about 5 ml to about 50 ml, or more. In one preferred embodiment, at least one reservoir is suitable for containing about 20 ml to about 40 ml of biological fluid. In some embodiments including a plurality of reservoirs, at least one of the more upstream reservoirs (e.g., the reservoir(s) receiving biological fluid before the downstream reservoir(s) receive the fluid), has a larger volume than the more downstream reservoir.

In some embodiments, containers 30-33 are commercially available flexible blood bags.

The system can include at least one connector, and typically includes a plurality of connectors. In the embodiment illustrated in the Figures, the system 100 includes at least three connectors, 3, 34, and 35, that each have at least three branches, e.g., the connectors can be in the form of Y- or T-connectors. Suitable connectors are known in the art.

The system can include one or more flow control devices such as a clamp, seal, valve, transfer leg closure, or the like. Typically, the system includes a plurality of flow

control devices, and they can be located within or on the conduits, the containers and/or the needles or the cannulas. For example, the Figures illustrate embodiments having showing a plurality of flow control devices wherein flow control device 6 comprises an in-line valve in conduit 4, and flow control devices 66 and 66A comprise clamps on conduits 5 and 8 respectively. The Figures also illustrate flow control device 666 comprising an in-line valve in a port in container 30. Other arrangements and types of flow control devices are also suitable. For example, in some other embodiments similar to those illustrated, flow control device 66 comprises an in-line valve in conduit 5 and/or a flow control device is interposed between connector 3 and needle 1.

The use of flow control devices, preferably a plurality of flow control devices, can be especially desirable for those embodiments where it is preferred that the first portion of biological fluid be prevented from contacting another fluid such as, for example, an anticoagulant, wherein the other (e.g., non-biological) fluid is contained in the system (e.g., in conduit 4 and/or container 30). Illustratively, the use of an in-line flow control device (that is initially closed) in conduit 4 can prevent anticoagulant in conduit 4 or container 30 from passing into the portion of the conduit between the control device (e.g., device 6) and connector 3, thus preventing anticoagulant from reaching conduits 2 and 5 while the system is being transported or otherwise handled. Accordingly, when biological fluid is subsequently introduced into the system, there is no residual anticoagulant (or essentially no residual anticoagulant) in conduit 2 and/or 5 that could contact the first portion of biological fluid.

A variety of suitable needles or cannulas 1 and 21 (e.g., as illustrated in Figure 1, shown with needle covers) are known in the art. Preferably, needle 1 comprises a phlebotomy needle. If desired, needle 21 can also comprise a phlebotomy needle. The needles 1 and/or 21 can be attached to the system as is known in the art. For example, the needles can be integrally attached, or attached via connectors, such as, for example, luer connectors. The needle can be attached to a conduit 8 interposed between the needle 21 and reservoir 20 as shown in Figure 1. Other configurations are encompassed by the invention. For example, in some variations of the illustrated embodiments, the device 200, 200A can include a connector directly attached to a reservoir 20 and/or 20A.

In some other embodiments, at least one collection device does not include needle or cannula. For example, the collection device as manufactured can be closed at the distal end (i.e., the end not connected to a conduit that allows biological fluid to enter the

device), and the filled reservoir can be accessed, (e.g., via puncture, cutting, or removing a cap) before removing at least some volume of the first portion of the biological fluid from the device. Illustratively, e.g., as shown in Figure 2, the second collection device 200A (that is initially hermetically sealed) can include a removable cap or cover 22, for allowing access to the collected biological fluid. At least one collection device can include one or more connectors, access ports, conduits, containers, and/or chambers, e.g., for ease of access to samples or subsets of the first portion of biological fluid in the device.

In accordance with any embodiments of the invention, at least one collection device 200, 200A can be arranged to provide multiple samples or subsets of the first portion of the biological fluid.

Alternatively, or additionally, the system can include a biological fluid collection arrangement, comprising a plurality of collection devices, arranged in series and/or in parallel fluid communication. The arrangement can include a plurality of collection devices to provide multiple samples or subsets of the first portion of the biological fluid. The arrangement can include additional elements such as conduits (preferably sealable conduits) and/or connectors.

In one embodiment of the collection arrangement including at least two collection devices in parallel fluid communication, a first subset (e.g., the first 10 ml collected from the donor) of the first portion of biological fluid is passed into the first collection device, and a second subset of the first portion (e.g., the next 10 ml collected from the donor) is passed into the second collection device, wherein the second subset does not pass into the first collection device. In another embodiment of the collection arrangement, including at least two collection devices in series fluid communication (e.g., as shown in Figure 2), a first portion of biological fluid is passed into the first device, and some volume of the first portion is passed from the first device into the second device. Since the collection arrangement can include three or more collection devices, the arrangement can include two or more collection devices in series fluid communication and/or two or more collection devices in parallel fluid communication. Preferably, in those embodiments wherein the collection arrangement includes a plurality of collection devices, at least two collection devices are capable of receiving biological fluid and being subsequently sealed while maintaining a closed sterile system. If desired, some or each of the additional collection devices (e.g., at least the third collection device), can be so sealed after receiving biological fluid.

With respect to collecting multiple samples, in some embodiments, after collecting the first portion of the biological fluid in the device 200, the conduit 5 and/or the reservoir 20 can be segmented, e.g., with clamps, rings, and/or seals, to isolate samples or subsets of the biological fluid in each segment. Device 200A, conduit 8 and/or reservoir 20A can be similarly segmented after receiving biological fluid. Alternatively, or additionally, the collection device 200, 200A can include a plurality of reservoirs.

If desired, individual segments, collection devices, compartments and/or reservoirs can be accessed (e.g., for testing), without compromising the sterility of the biological fluid in the other segments, devices, compartments and/or reservoirs.

The system 100 (as well as the collection device(s) 200, 200A) can, of course, include additional components such as, but not limited to, at least one additional conduit, container, connector, and flow control device.

In some embodiments, the system includes at least one filter (including, for example, at least blood filter, for example, at least one leukocyte depletion filter and/or an inactivating agent removal filter). For example, in one embodiment, the system includes at least one leukocyte depletion filter, e.g., for filtering red blood cells, platelet-rich-plasma, or platelet concentrate. Alternatively or additionally, embodiments of the system include at least one of a vent (including a gas inlet and/or a gas outlet), a gas collection and displacement loop, and a drip chamber. Other suitable components include, for example, a phlebotomist needle protection device.

An exemplary embodiment of a method according to the invention can be described with reference to Figure 1, that illustrates a closed biological fluid processing system 100. In one embodiment, the system contains fluid such as anticoagulant in conduit 4 and/or in container 30.

In accordance with this illustrated embodiment, needles 1 and 21 are initially capped, and flow control devices are closed before biological fluid (e.g., blood) is passed into the system 100.

Illustratively, a blood donor's arm is prepared for venipuncture in the usual manner, and needle 1 is uncapped and inserted into the donor's vein. Flow control device 66 (if present) is opened, and the first portion of the donor's blood (likely containing bacteria from the donor's skin) is passed into collection device reservoir 20 of first collection device 200. Since flow control device 6 is closed, blood is prevented from passing into receiving container 30.

In those embodiments wherein a fluid such as an anticoagulant is contained in the conduit 4, the use of flow control device 6 prevents this other fluid from contacting the first portion of biological fluid. Accordingly, the collected first portion of biological fluid in first collection device 200 is free of, or essentially free of, the other fluid. In one preferred embodiment, the collected blood is essentially free of anticoagulant. In those embodiments wherein flow control device 6 is an in-line valve, or wherein the system is shipped with another type of flow control device associated with conduit 4 (e.g., near connector 3) that is closed during shipment and/or handling of the system before use, the first portion of blood can be collected free of anticoagulant.

After a sufficient volume of blood passes into the collection reservoir 20, the conduit 5 is closed (e.g., clamped, for example, using flow control device 66), and typically sealed, e.g., at location 7. Typically, at least about 3 ml of blood is passed into the collection reservoir, more preferably at least about 10 ml of blood (for example, about 15 to about 30 ml, or more) is passed into the reservoir.

In some embodiments, the conduit 5 is closed and sealed essentially simultaneously. The conduit can be closed and/or sealed as is known in the art. In one embodiment, the conduit is sealed via a heat seal.

In a typical embodiment of the method, the second portion of biological fluid is passed into container 30, while maintaining the closed system, before further processing the first portion of biological fluid in reservoir 20.

Accordingly, flow control device 6 is opened, and a second portion of biological fluid, e.g., a unit of blood, is passed into container 30. This portion of blood is less likely to present a risk of significant bacterial contamination, since the greater number or increased level of bacteria associated with the donor's skin is likely to be passed with the first portion of blood into the first collection device 200.

After the second portion of biological fluid is passed into the container, the needle 1 is removed from the donor's vein, and the needle is handled as is known in the art. Typically, the needle is capped and/or placed in a phlebotomist protector device.

The first and second portions of biological fluid are typically further processed, as will be described in more detail below after describing another embodiment of the method with reference to Figure 2.

Figure 2 also illustrates a closed biological fluid processing system 100, including a biological fluid collection arrangement comprising first collection device 200 and second

collection device 200A (e.g., wherein second collection device 200A, connected to the system 100, is hermetically closed before use). As described above with respect to Figure 1, the system can contain fluid such as anticoagulant in conduit 4 and/or in container 30.

In accordance with the embodiment illustrated in Figure 2, needle 1 is initially capped, and flow control devices 6 and 66 are closed (flow control device 66A is also typically closed) before biological fluid, e.g., blood, is passed into the system 100. The donor's arm can be prepared, needle 1 uncapped and inserted, and a first portion of biological fluid can be passed into first collection device 200, as described above.

After conduit 5 is closed, and typically sealed, as described above, at least some of the volume of the first portion of biological fluid is passed from first collection device 200 into second collection device 200A. For example, flow control device 66A (associated with conduit 8) is opened, the opposing portions of walls 23 of reservoir 20A are compressed and released at least once (causing sterile air to pass from the reservoir 20A into reservoir 20), and some volume of the first portion of blood is passed into collection device reservoir 20A of collection device 200A. Since conduit 5 is closed, air (if present) is prevented from passing into conduit 2 (e.g., toward the donor). Additionally, since flow control device 6 is closed, blood from the donor is prevented from passing into receiving container 30.

After a sufficient volume of blood passes into the collection reservoir 20A, the conduit 8 between the first and second devices 200 and 200A is closed (e.g., using flow control device 66A), and typically sealed. Typically, the second portion of biological fluid is passed into container 30, while maintaining the closed system, before further processing the first portion of biological fluid in reservoir 20A.

With reference to the illustrated systems, in preferred embodiments of the method, the first portion of biological fluid is further processed, e.g., passed from the reservoir 20 (Figures 1 and 2) or reservoir 20A (Figure 2) after the first collection device 200 is separated from the rest of the system 100, although this can be carried out while device 200 remains attached to the rest of the system.

The collection device(s) 200, 200A (and the collection arrangement) can be separated from the rest of the system 100, preferably without compromising the sterility and integrity of the collection devices or the rest of the system 100. For example, the closed (e.g., sealed) conduits 5 and 8 can be cut, without compromising the sterility and integrity of the collection device(s) 200 and/or 200A or the rest of the system 100. The

collection devices can be separated from the rest of the system 100 before or after passing the second portion of biological fluid into the container 30. Since the collection devices can be separated from the rest of the system without compromising sterility and integrity, the collected biological fluid remains in a closed system, and the collected portion can be stored (e.g., for 2 days or more) if desired, before analysis and testing.

As noted earlier, the collection devices 200 and/or 200A can be arranged to provide multiple samples or subsets of the first portion of biological fluid. For example, after collecting the first portion of the biological fluid in the device 200 and/or 200A, at least one conduit (5 and/or 8) and/or at least one reservoir (20 and/or 20A) can be segmented, e.g., with clamps, rings, and/or heat seals, to isolate samples or subsets of the biological fluid in each segment. If desired, individual segments can be accessed (e.g., for testing), without compromising the sterility of the biological fluid in the other segments.

In accordance with the preferred embodiments of the invention, at least some volume of the first portion of the biological fluid (e.g., obtained as described above with respect to Figures 1 and 2) is passed from the collection device(s) 200 and/or 200A and analyzed and/or tested.

Since the biological fluid is collected in the collection devices while maintaining a closed system, the biological fluid can be stored until further use, e.g., analysis and/or testing. Typically, the analysis and/or testing of the first portion of biological fluid is carried out in an open system, e.g., after passing a volume of fluid through needle 21 (Figure 1) or after removing cap 22 (Figure 2).

In accordance with one embodiment of the invention (e.g., as shown in Figure 1), the first collection device 200 also includes at least one needle 21, preferably a needle suitable for penetrating the seal of a sampling device such as a vacutainer, and at least some of the volume of the first portion of biological fluid can be passed through the needle 21 into the sampling device. For example, the collection device 200 can be separated from the rest of the system 100 as described above (e.g., after heat-sealing and cutting conduit 5), and the cover over needle 21 can be removed. The needle is then inserted into the sampling device as is known in the art, and at least some of the volume of the first portion of biological fluid is passed into the device. The needle is disengaged after the desired volume of fluid is passed into the sampling device, and additional aliquots can be passed from the collection device (e.g., additional sampling devices can be filled) as

desired.

In accordance with other embodiments (e.g., as shown in Figure 2), at least one collection device (e.g., second collection device 200A) lacks a needle. After second collection device 200A is filled as described above (e.g., after passing some of the volume of the first portion of biological fluid from the first device 200 to the second device 200A), cap 22 (that can be a break off cap or a threaded cap) can be removed, allowing access to the collected fluid, and a least a portion of the fluid can be withdrawn. Alternatively, conduit 5 can be cut, and, in those embodiments wherein the wall 22 of reservoir 20 is resilient, portions of the wall can be compressed, causing fluid to be passed from the reservoir through the conduit into a container such as a test tube or cuvette. In accordance with yet another embodiment, a needle can be inserted into the collection device and at least one sample can be withdrawn. Other protocols for obtaining volumes of the first portion of biological fluid from the collection device are also encompassed by the present invention.

The separated volume of the first portion of biological fluid can be analyzed and/or tested as is known in the art. Illustrative analyses and tests include for example, but are not limited to, blood typing, blood component viability tests, blood component counts, serology tests, drug tests, diagnostic tests, tests for infectious diseases and/or viruses, liver enzymes. Other suitable analyses and tests (including automated protocols) are known to one of ordinary skill in the art.

If desired, the second portion of biological fluid (in receiving container 30), that is obtained while maintaining the closed system, is further processed, e.g., separated into components, stored, and/or filtered, as is known in the art. For example, in those embodiments wherein the second portion of biological fluid is a unit of blood, the blood can be separated into components such as packed red blood cells, platelet-rich-plasma, platelet concentrate, and plasma, and any of the components can be passed through a suitable leukocyte depletion filter.

Illustratively, the biological fluid collected in container 30 can be centrifuged, flow control device 666 can be opened, and blood components of different densities can be sequentially passed along conduit 9 into one or more different containers. For example, flow control devices associated with the appropriate conduits can be operated as is known in the art, and platelet-rich-plasma (PRP) can be passed along conduits 9, 11 and 12 into container 32, leaving concentrated red cells in container 30. The PRP can be further

processed to form platelet concentrate (remaining in container 32) and platelet-poor-plasma, that is passed from container 32 along conduits 12 and 13 into container 33. Additive solution (e.g., red cell additive solution) can be passed from container 31 along conduits 10 and 9 into container 30. If desired, the components can be leukocyte-depleted, for example, by passing them through leukocyte depletion filters interposed between the various containers, or by subsequently passing the separated components through filters.

Since the presence of bacteria in the second portion of biological fluid is reduced, and the second portion of biological fluid is obtained while maintaining the closed system, embodiments of the present invention are particularly suitable for storing and pooling blood components, particularly components such as platelets, that are stored under conditions that are conducive to reproduction of bacteria.

For example, a plurality of units of biological fluid (e.g., donated blood) can be obtained as described above, e.g., wherein the first portion of each donation is passed into a collection device, and wherein the second portion of each donation is passed into a first container. The second portions can be further processed to separate one or more components of interest, e.g., platelets and/or red blood cells, and the separated components can be stored for a suitable storage period. If desired, the separated components (e.g., units of platelets such as platelet concentrate) can be pooled before use as a transfusion product. In accordance with embodiments of the invention, the separated components can be pooled before or after storage.

EXAMPLE

The example describes one embodiment of a method according to the invention, wherein first portions of blood are obtained in a closed system, while minimizing bacterial contamination of the remaining collected blood.

A system is arranged as generally shown in Figure 1 (without the additional components communicating with container 30). The system 100, which is a closed sterile system, includes a phlebotomy needle 1 with a needle cover, conduits 2, 4, 5, and 8, Y-connector 3, blood receiving bag 30, collection device 200, collection device reservoir 20, and needle 21 with a needle cover. A conduit is interposed between needle 21 and reservoir 20, and provides fluid communication between the needle and the reservoir. The system also includes a frangible in-line valve 6, and optional clamps 66 and 66A.

Collection device reservoir 20 and blood receiving bag 30 are produced from flexible plastic films.

The system, that contains some amount of anticoagulant in conduit 4 and blood receiving bag 30, is sterilized. The valve 6, as well as clamps 66 and 66A are closed before blood is passed into the system. A blood donor's arm is prepared for venipuncture as is known in the art, and the phlebotomy needle is inserted into the donor's vein. Clamp 66 is opened, and clamp 66A and in-line valve 6 remain closed. Since valve 6 is closed, anticoagulant is prevented from passing into conduit 2.

The first portion of the donor's blood, that contains bacteria from the donor's skin (and possibly the donor's bacteria-containing skin plug) passes into collection device 200. Since valve 6 remains closed, blood does not pass into the blood receiving bag 30, and anticoagulant in the tubing 4 neither contacts the blood nor passes into the collection device 200.

After the first portion of blood (i.e., about 15 ml of blood) passes into the collection device reservoir 20, clamp 66 is closed, and the tubing 5 is heat-sealed, while maintaining a closed system. Valve 6 is opened, and a second portion of blood, e.g., a unit of blood, is collected into blood receiving device 30. This portion of blood is less likely to present a risk of significant bacterial contamination, since the greater number of bacteria associated with the donor's skin are likely to be passed with the first portion of blood into the collection device 20.

The sealed collection device 200 is separated from the rest of the system 100 while maintaining the closed nature of both the device 200 and the remaining part of the system. After tubing 5 is heat sealed, the tubing is cut without compromising the seal at the ends of the tubing.

The needle cover over needle 21 is removed and the tip of the needle is inserted into a stoppered evacuated blood collection tube, clamp 66A is opened, and at least some volume of the first portion of the blood is passed into the tube for analysis of bacterial contamination. Additionally, at essentially the same time, a volume of the second portion of blood is analyzed for bacterial contamination.

The first portion of blood (from the initially collected 15 ml) is found to be contaminated with Staphylococcus epidermidis, and the second portion is not found to be contaminated with Staphylococcus epidermidis. This example shows that contamination of collected blood with Staphylococcus epidermidis can be reduced by separately collecting a

first portion of blood.

All of the references cited herein, including publications, patents, and patent applications, are hereby incorporated in their entireties by reference.

While the invention has been described in some detail by way of illustration and example, it should be understood that the invention is susceptible to various modifications and alternative forms, and is not restricted to the specific embodiments set forth. It should be understood that these specific embodiments are not intended to limit the invention but, on the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the invention.

What is claimed is:

1. A system for processing a biological fluid comprising:

a biological fluid collection device for receiving a first portion of a biological fluid from a source of the biological fluid, said device being capable of being sealed after receiving the first portion, while maintaining a closed system;

at least a first container for receiving a second portion of a biological fluid from the source of the biological fluid;

wherein the biological fluid collecting device and the first container are in fluid communication with the source of the biological fluid.

2. The system of claim 1, including at least one additional biological fluid collection device, in fluid communication with the first biological fluid collection device, wherein the additional biological fluid collection device is capable of receiving biological fluid and being sealed while maintaining a closed system.

3. The system of claim 1, including a connector having at least three branches capable of passing fluid therethrough, said connector being interposed between, and in fluid communication with, the source of the biological fluid, the biological fluid collecting device, and the first container.

4. The system of any preceding claim, including a heat-sealable conduit interposed between the connector and the biological fluid collecting device.

5. The system of claim 2, wherein at least one additional biological fluid collection device includes a reservoir having at least one side wall having a resilient portion.

6. A method for processing a biological fluid comprising:

passing a first portion of a biological fluid into a collecting device capable of being sealed, after receiving the first portion, while maintaining a closed system; and

passing a second portion of the biological fluid into a container, while maintaining the closed system.

7. The method of claim 6, including sealing the first portion of biological fluid in the

collecting device while maintaining a closed system before passing the second portion of the biological fluid into the container.

8. The method of claim 6 or 7, wherein the first portion of biological fluid collected in the collecting device is essentially free of anticoagulant.

9. An arrangement for processing biological fluid comprising:

a first device including a biological fluid reservoir for receiving a portion of a biological fluid; and

a second device including a biological fluid reservoir for receiving a portion of a biological fluid, said second device being capable of fluid communication with the first device;

wherein the first device is arranged to receive a first portion of a biological fluid in a closed system; and wherein the first and second devices are capable of being sealed after receiving biological fluid while maintaining a closed system.

10. The arrangement of claim 9, wherein the first and second devices are in fluid communication in series, and the second device is arranged to receive at least some volume of the first portion of biological fluid from the first device.

11. The arrangement of claim 9 or 10, further comprising at least one additional device including a biological fluid reservoir for receiving a portion of a biological fluid.

12. The arrangement of any one of claims 9-11, wherein the second device is arranged to be sealed while maintaining a closed system after receiving the a volume of the first portion of biological fluid from the first device.

13. The arrangement of any one of claims 9-12, wherein at least one reservoir is flexible.

14. The arrangement of any one of claims 9-12, wherein at least one reservoir has at least one side wall including a resilient portion.

15. The system of claim 1, wherein the biological fluid collection device is suitable for

receiving at least about 10 ml of biological fluid.

16. The system of claim 15, wherein the biological fluid collection device is suitable for receiving at least about 25 ml of biological fluid.

17. The method of any of claims 6-8, comprising passing at least about 10 ml of biological fluid into the biological fluid collection device.

18. The method of claim 17, comprising passing at least about 25 ml of biological fluid into the biological fluid collection device.

19. The method of any preceding claim, further comprising passing some of the volume of the first portion of the biological fluid from the biological fluid collection device to an additional biological fluid collection device, while maintaining a closed system.

20. The method of any of claims 7-9, 18, and 19, further comprising passing additional biological fluid from the source of the biological fluid into an additional biological fluid collection device.

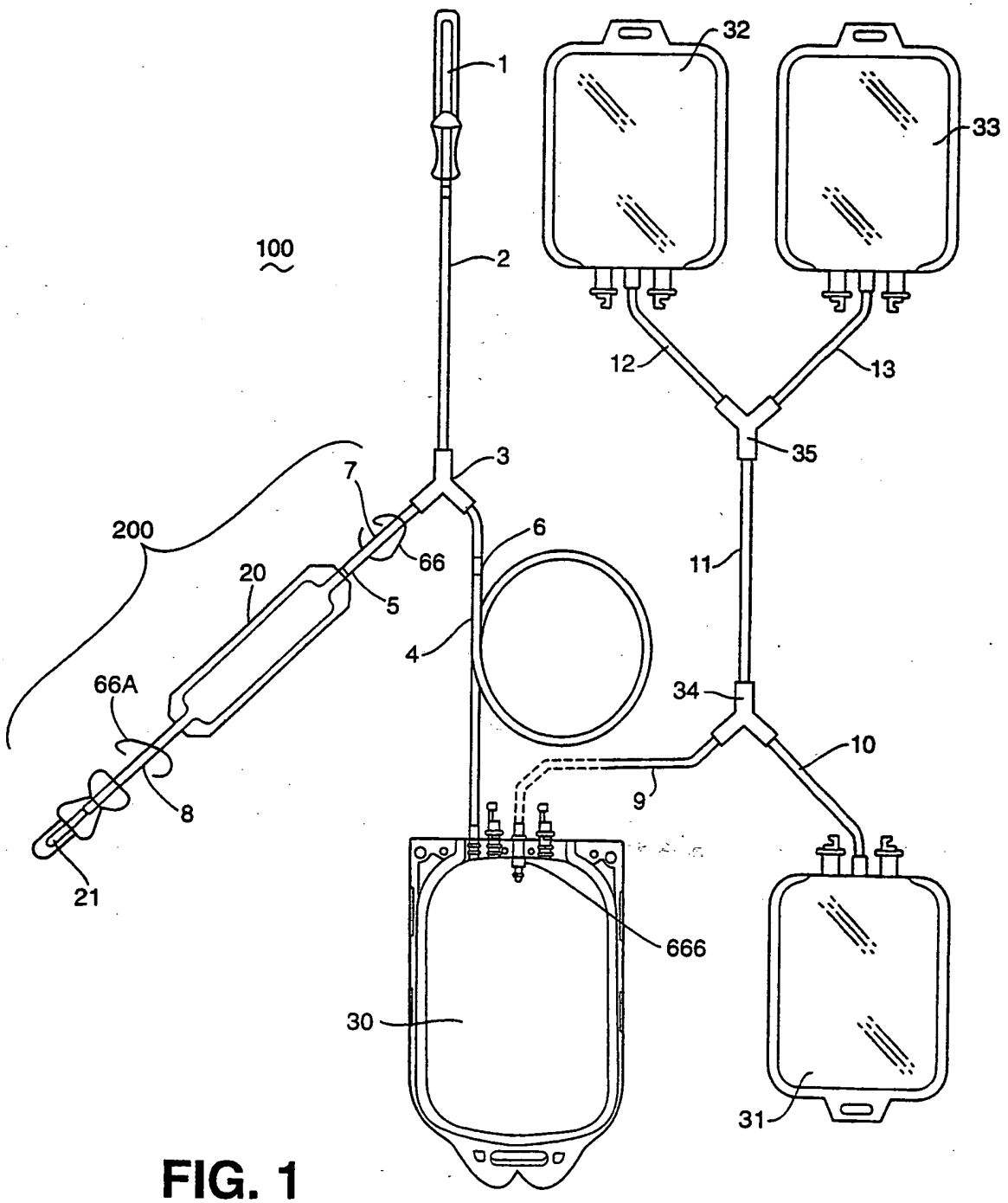

FIG. 1

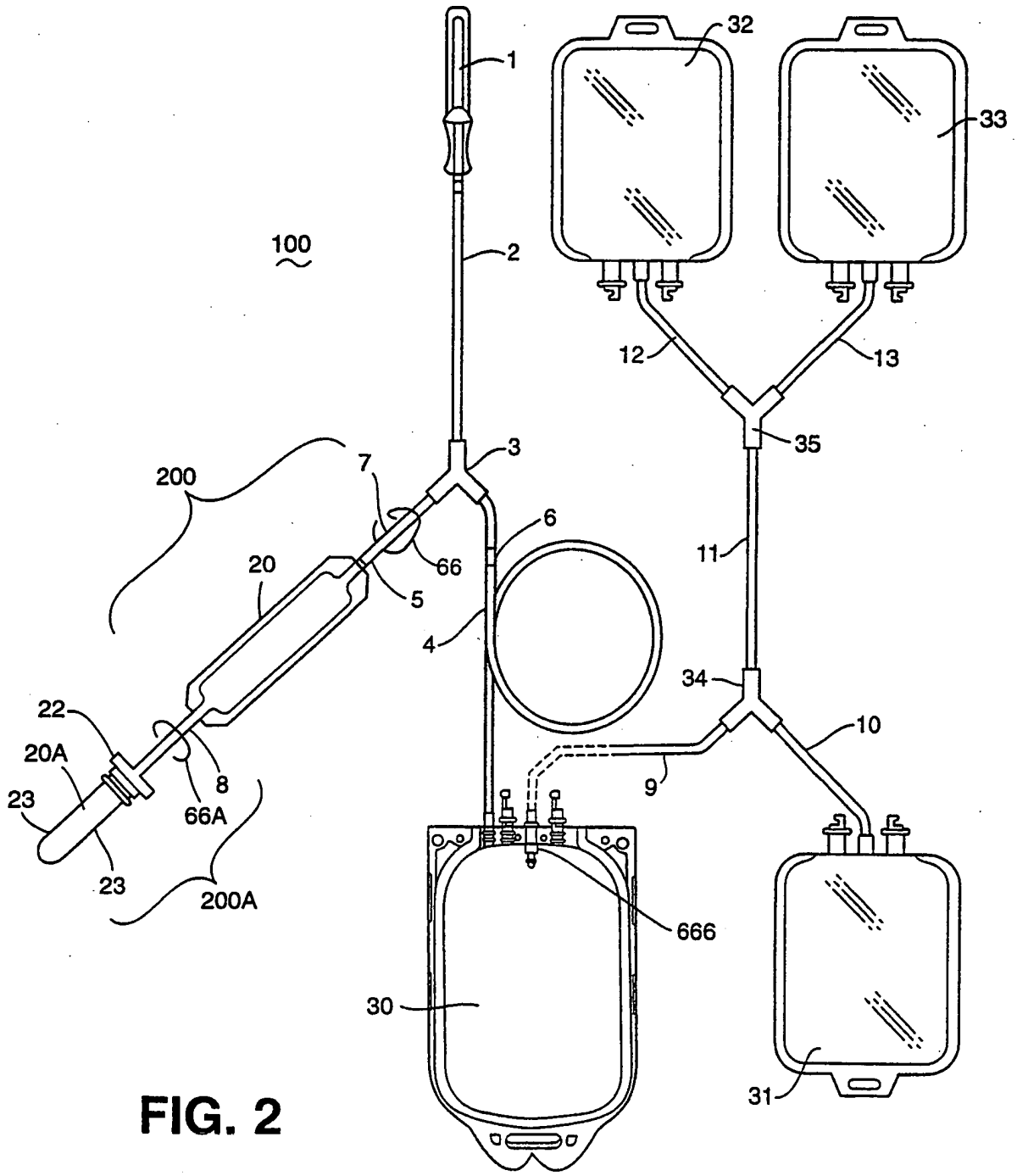
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FIG. 2

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/17174

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M1/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 83 01573 A (BAXTER TRAVENOL LAB) 11 May 1983 (1983-05-11) page 15, line 26 -page 17, line 26 page 19, line 13 - line 24 page 22, line 21 -page 23, line 11 page 23, line 24 -page 24, line 6 page 33, line 26 -page 34, line 3 figure 1 ---	1-7,9-20
X	WO 92 12684 A (BAXTER INT) 6 August 1992 (1992-08-06) page 6, line 19 -page 8, line 26 figure 1 --- -/--	1,2,5-7, 9-15, 17-20

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 November 1999	18/11/1999

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

national Application No
PCT/US 99/17174

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 142 240 A (TERUMO CORP) 16 January 1985 (1985-01-16) abstract figure 3	1,3,4,6, 7,9, 12-18
X	US 2 950 716 A (BELLAMY DAVID JR, WALTER CARL W) 30 August 1960 (1960-08-30) column 2, line 9 - line 32 column 3, line 14 - line 29 column 4, line 46 -column 5, line 9 figure 1	1,6-9, 12-17
P,X	EP 0 930 079 A (TERUMO CORP) 21 July 1999 (1999-07-21) paragraphs '0013!,'0016!,'0030!,'0033!,'0038!,'0048!, '0103!,'0172! figures 1,4	1-9, 11-15, 17,20

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/17174

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8301573 A	11-05-1983	AR 229134 A	15-06-1983
		AU 8952082 A	18-05-1983
		BR 8207948 A	20-09-1983
		EP 0093122 A	09-11-1983
		ES 516895 A	01-02-1984
		JP 58501807 T	27-10-1983
WO 9212684 A	06-08-1992	US 5167656 A	01-12-1992
		AU 642080 B	07-10-1993
		AU 1224992 A	27-08-1992
		CA 2076677 A	23-07-1992
		EP 0521129 A	07-01-1993
GB 2142240 A	16-01-1985	CH 662276 A	30-09-1987
		DE 3413692 A	24-01-1985
		DE 8411408 U	28-04-1988
		FR 2548905 A	18-01-1985
		SE 461379 B	12-02-1990
		SE 8402023 A	28-12-1984
		US 4846795 A	11-07-1989
US 2950716 A	30-08-1960	DE 1138186 B	
		FR 1171493 A	27-01-1959
		GB 829656 A	
EP 0930079 A	21-07-1999	JP 11197236 A	27-07-1999